UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

4/6/89

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Histopathology Report on 2,4-Dichlorophenoxyacetic Acid Rat Studies

FROM: Lynnard J. Slaughter L. J. S.
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Health Effects Division (H7509C)

TO: Marcia Van Gemert, Ph.D., Acting Chief
Review Section II
Toxicology Branch II
Herbicide, Fungicide and Antimicrobial Support
Health Effects Division (H7509C)

I have reviewed the following documents provided me; they are:

1. Memorandum dated October 20, 1986

   SUBJECT: REVIEW OF THE HISTOPATHOLOGY TABLES SUBMITTED ON 2,4-D

2. Memorandum dated December 15, 1986

   SUBJECT: DR. SWENBERG'S EVALUATION OF THE BRAIN SLIDES FOR THE 2,4-DICHLOROPHENOXYACETIC ACID RAT STUDY

3. Memorandum dated June 30, 1986

   SUBJECT: PRELIMINARY REVIEW OF COMBINED TOXICITY AND ONCOGENICITY STUDY IN RATS ON 2,4-DICHLOROPHENOXYACETIC ACID

4. Memorandum dated March 27, 1987

   SUBJECT: REVIEW OF THE MOUSE ONCOGENICITY STUDY ON 2,4-DICHLOROPHENOXYACETIC ACID

5. Memorandum dated July 15, 1988

   SUBJECT: REVIEW OF COMMENTS ON 2,4-DICHLOROPHENOXYACETIC ACID PROPOSAL NOT TO INITIATE A SPECIAL REVIEW

6. Pathology Report Review

   SUBJECT: DYNAMAC CORPORATION STUDY NO. HLA 2184-102 SUBCHRONIC STUDY OF 2,4-D IN RATS
   Pathology Report Submitted
   January 16, 1989

7. Pathology Report Review

   SUBJECT: DYNAMAC CORPORATION STUDY NO. HET K-002372-22 SUBCHRONIC STUDY OF 2,4-D IN RATS
   Pathology Report Submitted
   January 16, 1989

8. Pathology Report Review

   SUBJECT: DYNAMAC CORPORATION STUDY NO. HLA 2184-103 CHRONIC STUDY OF RATS FED 2,4-D
   Pathology Report Submitted
   January ?, 1989

9. MEMORANDUM DATED AUGUST 7, 1984
   DOCUMENT NO. 3888
   FROM: HANK SPENCER TO: RICHARD MOUNTFORT

   A report which includes clinical pathology data

eneral Comments

1. The kidney lesion described and discussed in the above-mentioned reports are not life threatening nor are they biologically important with respect to these animals' consumption of 2,4-D. These lesions are consistent with those found in aging rats. Whether or not the chemical in question influenced

the early onset of a naturally occurring disease process cannot be deduced from animals subjected to the experimental design that was used for these studies.

2. It is reasonable to expect that in life threatening situations, one or more appropriate organ function tests (kidney in this case) must be evaluated before it be concluded the animals' kidneys have failed or are failing. The following kidney function tests (clinical pathology) data presented in the original bioassay reports indicate that the blood urea nitrogen levels in these animals was decreased at the 14 mg and the 45 mg dose levels.

   The urinalysis, chemical and microscopic data of these animals needs evaluating. Also, the total protein, total bilirubin, total cholesterol, SGOT and the SGPT serum values from the animals likewise need evaluating.

3. In regards to the astrocytomas found in the brains of the animals consuming 2,4-D, a more careful analysis of scientific literature reports of the spontaneous incidence of this tumor's occurrence in this rat strain may be advisable before another study is initiated.

4. Following my recent telephone conversation with Dr. Banas of E.P.L., I believe it can be concluded that:

   a. Two hundred ninety-eight pairs of male kidneys were histologically evaluated of an expected 300 pairs of kidneys;

   b. Three hundered pairs of female kidneys were histologically evaluated of an expected 300 pairs of kidneys;

   c. Although a few kidneys were autolytic, it was not severe enough to prohibit the histopathological evaluation of the lesion identified;

   d. We agree that the lesions identified in the kidneys are not life threatening and this is supported by the study blood urea nitrogen values (mg/100 mL) in these animals; see document 3888 mentioned above;

e. The kidney lesions identified in the above-mentioned pathology reports of test and control rat, are commonly observed in 18- to 24-month-old animals that are progressively developing spontaneous chronic renal disease; the etiology of which remains unclear.

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R120354

Chemical: 2-4,D

PC Code:
030001
HED File Code: 13000 Tox Reviews
Memo Date: 4/6/1989
File ID:
Accession #: 412-06-0013

HED Records Reference Center
2/27/2006